



[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Announcement of a Draft NIH Policy on Dissemination of NIH-Funded Clinical Trial Information

SUMMARY: On November 19, 2014, the National Institutes of Health (NIH) published a request for public comments in the NIH Guide for Grants and Contracts on a draft policy to promote broad and responsible dissemination of information on clinical trials funded by the NIH through registration and submission of summary results information to ClinicalTrials.gov. See Guide notice NOT-OD-15-019 at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-019.html>. NIH is publishing this notice in order to inform readers of the Federal Register about the draft policy and the opportunity to comment.

DATES: The deadline for receiving comments on the draft policy is no later than 5:00 p.m. on March 23, 2015.

ADDRESSES: Comments may be submitted by any of the following methods:

- Email: clinicaltrials.disseminationpolicy@mail.nih.gov
- Fax: 301-496-9839
- Mail/Hand delivery/Courier: Office of Clinical Research and Bioethics Policy, Office of Science Policy, National Institutes of Health, 6705 Rockledge Drive, Suite 750, Bethesda, MD 20892.

FOR FURTHER INFORMATION CONTACT: Office of Clinical Research and Bioethics Policy, Office of Science Policy, National Institutes of Health, 6705 Rockledge Drive, Suite 750, Bethesda, MD 20892, 301-496-9838, OCRBP-OSP@od.nih.gov.

SUPPLEMENTARY INFORMATION:

Background

The National Institutes of Health (NIH) is dedicated to improving the health of Americans by conducting and funding biomedical and behavioral research, including clinical trials.¹ A fundamental premise of all NIH-funded research is that the results of such work must be disseminated in order to contribute to the general body of scientific knowledge and, ultimately, to the public health. NIH awardees are expected to make the results and accomplishments of their activities available to the research community and to the public at large.

The results of NIH funded research can be disclosed in a number of ways, including through publications, presentations at scientific meetings, sharing research tools, and depositing information into databases and materials into repositories. NIH has a number of policies that promote the dissemination of research results and guide funding recipients in disseminating their results. The NIH Data Sharing Policy, the NIH Public Access Policy, the NIH Research Tools Policy, and the NIH Genomic Data Sharing Policy are important examples of policies to ensure that research data and materials generated using NIH funds are used productively to further scientific progress and to promote public health.² Increasing public access to information from

¹ NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. See <http://www.nih.gov/about/mission.htm>.

² See http://www.grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm; <http://publicaccess.nih.gov/>; http://grants.nih.gov/grants/intell-property_64FR72090.pdf; and <http://gds.nih.gov/03policy2.html>.

NIH research supports the public access and data sharing directives of the Executive Office of the President (EOP Directives).³

Traditionally, scientists fulfill their obligation to contribute to the general body of knowledge through peer reviewed journal publications. However, journal publication is not always possible, and many clinical trials are not being published or published in a timely manner. A recent study found that the results of less than half of NIH-funded clinical trials had been published in a peer-reviewed biomedical journal within 30 months of trial completion.⁴ Selective publication of the results of some trials and not others – or publication of incomplete or partial findings from a particular trial – can lead to inappropriate conclusions about the usefulness of particular therapies.⁵

Public access to clinical trial information drives scientific progress and optimizes the return on the nation’s investment in clinical trials. It helps inform future research, improve study design, and prevent duplication of unsafe and unsuccessful trials. In addition, there is an important ethical dimension to dissemination of clinical trial results because individuals who volunteer to participate in such studies, and who may assume risks, trust that what we learn will contribute to generalizable knowledge about human health. Finally, enhancing transparency also increases public trust in clinical research. It is, therefore, important to provide other ways for clinical trial results to be disseminated and publicly available to researchers, health care providers, and patient communities.

³ See the Office of Science and Technology Policy’s memorandum, “Increasing Access to the Results of Federally Funded Scientific Research,” (February 22, 2013), the Office of Management and Budget’s memorandum, “Open Data Policy—Managing Information as an Asset,” M-13-13 (May 9, 2013) <http://www.whitehouse.gov/sites/default/files/omb/memoranda/2013/m-13-13.pdf>, and Executive Order No. 13,642 (May 9, 2013) <http://www.gpo.gov/fdsys/pkg/DCPD-201300318/pdf/DCPD-201300318.pdf>.

⁴ Ross JS, Tse T, Zarin DA, Xu H, Zhou L, Krumholz HM. Publication of NIH funded trials registered in ClinicalTrials.gov: cross-sectional analysis. *BMJ*. 2012;344:d7292.

⁵ Nissen S, Biomarkers in Cardiovascular Medicine, The Shame of Publication Bias, *JAMA Intern Med* 2013 March 25; doi:10.001/jamainternmed.2013.4074; Dwan K et al., Systematic review of the empirical evidence of study publication bias and outcome reporting bias, *PLoS One* 2008 Aug 28;3(8):e3081. doi: 0.1371/journal.pone.0003081; Begg C, Berlin J, Publication bias and dissemination of clinical research, *J Natl Cancer Inst* 1989, Jan 18;81(2):107-15.

Some NIH-funded clinical trials are subject to mandatory registration and reporting of results under federal law, i.e., Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA). FDAAA applies, in general, to controlled, interventional studies of Food and Drug Administration (FDA)-regulated drugs, biological products, and devices, excluding phase 1 studies of drugs and biological products and small feasibility studies of devices. Under FDAAA, a minimal set of summary information about such clinical trials must be submitted in a structured, tabular format to ClinicalTrials.gov, a freely accessible and searchable registry and results data bank operated by the National Library of Medicine (NLM), NIH.

NIH is proposing to issue a policy to ensure that all NIH-funded clinical trials are registered and have summary results, including adverse event information, submitted to ClinicalTrials.gov. Compliance with this policy will be a term and condition in the Notice of Grant Award and a contract requirement in the Contract Award. This proposed policy supports the NIH mission and is essential to facilitate the translation of research results into knowledge, products, and procedures that improve human health.

Request for Comments

NIH encourages the public to provide comments on any aspect of the draft policy, described below. Comments should be submitted electronically to the Office of Clinical Research and Bioethics Policy (OCRBP), Office of Science Policy, NIH, via email at email at clinicaltrials.disseminationpolicy@mail.nih.gov, mail at 6705 Rockledge Drive, Suite 750, Bethesda, MD 20892, or by fax at 301-496-9839. Submitted comments are considered public information; private or confidential information should not be submitted. Comments may be posted along with the submitter's name and affiliation on the OCRBP web site after the public comment period closes.

Draft NIH Policy on Dissemination of NIH-Funded Clinical Trial Information

Purpose. The purpose of this Policy is to promote broad and responsible dissemination of information from NIH-funded clinical trials through ClinicalTrials.gov, the clinical trial registry and results databank operated by the National Library of Medicine (NLM). Disseminating this information supports the NIH mission to advance the translation of research results into knowledge, products, and procedures that improve human health. This Policy is intended to complement the statutory mandate under Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) that requires registration and submission of summary results for certain clinical trials, whether funded by NIH or by other entities, to be registered and have summary results submitted to ClinicalTrials.gov.⁶

Scope and Applicability. This Policy applies to all NIH-funded awardees and investigators conducting clinical trials, funded in whole or in part by NIH, regardless of study phase, type of intervention, or whether they are subject to the FDAAA registration and results submission requirements set forth in Section 402(j) of the Public Health Service Act (42 U.S.C. 282(j)). For purposes of this Policy, a clinical trial is defined as “a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes⁷.”

⁶ The mandate applies to certain “applicable clinical trials” (ACTs) of drugs (defined by section 402(j)(1)(A)(vii) of the Public Health Service Act to include biological products) and devices, including any pediatric postmarket surveillance of a device required by FDA under section 522 of the Federal Food, Drug, and Cosmetic Act (FD&C Act). See 42 U.S.C. 282(j).

⁷ Several terms within the NIH definition of clinical trial definition mean are defined as follows. “Research” and “human subject” are defined in the Common Rule at 45 CFR 46.102(d) and 45 CFR 46.102(f), respectively. “Prospectively assigned” refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo or other control) of the clinical trial. An “intervention” is defined as a manipulation of the subject or subject’s environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior

Effective Date. This Policy is effective for:

- Competing grant applications that include clinical trials and are submitted to the NIH for the [date to be determined] receipt date and subsequent receipt dates;
- Proposals for contracts that include clinical trials and are submitted to the NIH on or after [date to be determined]; and
- NIH intramural research projects that include clinical trials for which Institutional Review Board review is initiated after [date to be determined].

Responsibilities. As set forth in the terms and conditions of grant and contract awards, all NIH-funded awardees and investigators conducting clinical trials, funded in whole or in part by NIH, who have committed to NIH that they will comply with NIH policies, are expected to ensure that their NIH-funded clinical trials are registered and summary results, including adverse event information, are submitted to ClinicalTrials.gov in accord with the timelines that will be set forth at ClinicalTrials.gov. Generally, this means registration of the clinical trial not later than 21 days after enrollment of the first participant and submission of summary results information not later than one year after the completion date. “Completion date” is defined to be the date that the final subject was examined or received an intervention for the purpose of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated. It will be possible to delay results submission for up to two years beyond the

(e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies. A “health-related biomedical or behavioral outcome” is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects’ biomedical or behavioral status or quality of life. Examples include positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and/or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life. See <http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/clinical-trials>

initial deadline with a certification that regulatory approval of the product is being sought.

Clinical trials covered by the policy will be expected to submit the same type of registration and results data and in the same timeframes as the trials subject to FDAAA. The specific registration and results information to be submitted will be made available at the ClinicalTrials.gov site.

Institutions and investigators should submit information directly to ClinicalTrials.gov. If the trial is subject to FDAAA, i.e., section 402(j) of the Public Health Service Act (42 U.S.C. 282(j)), submissions must be made by the Responsible Party, as defined at 42 U.S.C. 282(j)(1)(A)(ix). If an NIH-funded clinical trial is also subject to FDAAA, it needs to have only one entry in ClinicalTrials.gov that contains its registration and results information. Investigators and funding recipients are expected to cooperate with NLM to address any data curation or quality control issues to facilitate timely posting.

In general, NIH expects to make clinical trial registration and results information publicly available through ClinicalTrials.gov within 30 days after receipt by ClinicalTrials.gov.⁸ For NIH-funded trials that are subject to section 402(j) of the Public Health Services Act (42 U.S.C. 282(j)), submitted information will be posted in compliance with the relevant requirements of that section.

⁸ For clinical trials funded through SBIRs, the timeframe for posting results will be consistent with the SBIR Policy Directive, which generally prohibits the agency from posting SBIR data for at least 4 years from completion of the study unless the awardee consents to an earlier release. See SBIR Policy Directive, Sections 8(b)(2) and (4).

Failure to comply with the terms and conditions of NIH awards may provide a basis for enforcement actions, including termination, consistent with 45 CFR 74.62 and/or other authorities, as appropriate.⁹

Dated: January 8, 2015.

Lawrence Tabak, D.D.S., Ph.D.

Principal Deputy Director

National Institutes of Health

[FR Doc. 2015-02994 Filed 02/12/2015 at 8:45 am; Publication Date: 02/13/2015]

⁹ When the final policy is issued, NIH will also provide more specific procedural guidance to facilitate implementation.